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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,008	05/06/2002	Steven K Libutti	14014.0322U2	3848

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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,008	LIBUTTI ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/25/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19, 21-37, and 39* is/are pending in the application.

4a) Of the above claim(s) *3,5-15,17,19,23-37 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,16,18,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/15/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-22, the species of an adenovirus nucleic acid and the species of endostatin, in the reply filed on 11/25/2005 is acknowledged. The traversal is on the ground(s) that the reference applied in the restriction requirement (Tanaka et al) does not teach the special technical feature of the claims as amended (the claims were amended to include an adenoviral signal sequence). This is not found persuasive because the special technical feature of the amended claims (i.e. claim 1) is not considered a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art. See the U.S.C. 102(b) rejection below.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3, 5-15, 17, 19, 23-37 and 39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/25/2005.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: although original claim 38 provides support, there is no antecedent basis in the specification for the term "adenoviral signal sequence". It is suggested that the phrase be introduced into the specification on page 23, before the mention of the adenoviral E19 signal sequence.

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Pages 23, 40, 41, and 44 of the specification and claim 22 contain sequences not identified by a SEQ ID number. Furthermore, the nucleic acid sequence on page 44, line 10, is not found within the submitted sequence listing. These details are requirements of the Sequence Rules (MPEP 2400 §1.821-1.825) and must be corrected. Any response which does not include compliance with the Sequence Rules will be considered non-responsive.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 18, 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Restifo et al (U.S. patent 5,733,548, March, 1998) as evidenced by Tandle et al (J. Trans. Med., 2004). Restifo et al disclose a protein comprising the E19 signal sequence (as recited in the

instant claim 22) operatively linked to the P1A tumor peptide (see column 5, lines 40-44, SEQ ID NO: 7). Genes encoding the above fusion protein (and others) were inserted into the vaccinia virus TK gene (column 10, line 50 - column 11, line 32, and Example 1) and used to produce vaccinia virus particles bearing the fusion proteins for immunization and gene transfer (Examples 2 - 5). Vaccinia particles bearing a sequence encoding the E19/P1A fusion protein could induce an immune response which lysed P815 tumor cells (Example 5 and Figure 5), and thus the E19/P1A fusion protein is considered to be an antiangiogenic protein. This is because the term "antiangiogenic protein" is interpreted broadly, lacking a specific definition in the specification. Guidance on the interpretation of this term is taken from Tandle et al (J. Trans. Med., 2004), Figure 1, which indicates angiogenic inhibitors, in the context of antiangiogenic gene therapy, include direct and indirect inhibitors. Included in the indirect inhibitors are inhibitors of tumor cells, which prevent the expression of angiogenic growth factors and receptors. Thus, Restifo et al, by lysing p815 tumor cells (or any other tumor cell) using the E19/P1A fusion protein, inhibit tumor cells. This inhibition indirectly inhibits angiogenesis, and therefore the E19/P1A protein is considered an antiangiogenic protein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1, 2, 4, 16, 18, 21 and 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al (U.S. patent 6,638,502) in view of Restifo et al (as above).

Li et al teaches adenoviral vectors for the gene therapy of cancer that express antiangiogenic proteins such as the amino terminal fragment of urokinase, angiostatin, and endostatin. See Figs 1 and 7 and column 16, lines 12-15. The antiangiogenic proteins are operatively linked to the signal sequences (or signal peptide) of uPA (column 21, lines 22-24) or plasminogen (column 5, lines 55-56 and Fig. 7). The adenoviral vectors for foreign gene expression are replication-defective, see the ΔE1 vectors (Figs. 1A and 7A). Thus, Li et al teaches the claimed invention except for the adenoviral E19 signal sequence.

The teachings of Restifo et al are described above and applied as before. Restifo et al does not specifically teach the use of endostatin.

The claimed recombinant nucleic acids are essentially disclosed by both Li et al and Restifo et al, with the exception of endostatin (Restifo) and the E19 signal sequence (Li). The ordinary skilled artisan, seeking a composition to treat cancer, would have been motivated to use endostatin with the compositions taught by Restifo et al because Li et al teaches endostatin to be

a well known and desirable type of antiangiogenic protein having utility for preventing tumor growth. Conversely, the same artisan would have been motivated to use the E19 signal sequence of Restifo et al with the adenoviral vectors of Li et al because Restifo teaches the E19 sequence to be a well-known and functional secretion signal, and Li et al teaches the interchangeability of different signal sequences to secrete the desired antiangiogenic protein. It would have been obvious for the skilled artisan to do this because of the known benefit of generating compositions for expressing antiangiogenic proteins for cancer therapy as taught by Li et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Michael D. Burkhart
Examiner